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Growing Up with Extraordinary Challenges:

Hoping for the Best in Uncertainty

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Abstract

This essay presents a need and justification for an emerging field of study of the biological foundation of child's reaction to human adversity. It first discusses the connection between early adversity and child developmental outcomes. Then it mentions the presence of the remarkable amount of individual differences present in the outcome of previously institutionalized children as a result of adoption. Finally, it questions why such a powerful effect as early adversity is associated with such a tremendous amount of individual differences and suggests that this diversification can be related to the action of the epigenome.

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Researchers have investigated the associations between individual differences in early care and adult outcomes. And, in fact, it has been shown indisputably that the quality of early care is tightly connected to corresponding offspring developmental outcomes. Generally speaking, high-quality early care is associated with a range of positive outcomes, and low-quality early care with a host of negative outcomes.

Correspondingly, early adversity—when the quality of early care is severely challenged by negative environmental or situational factors—places children at elevated risk for maladaptive physical- and mental-health outcomes in adolescence and adulthood. Specifically, and most importantly for the context of this brief essay,

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early neglect has been strongly associated with unfortunate physical-health outcomes such as lung disease, peptic ulcers, arthritic disorders, diabetes, and autoimmune disorders [1], as well as cardiovascular malfunctioning [1], [2] and problematic mental-health outcomes such as depression [2], [3], anxiety [3], psychosis [4], aggression [5], drug abuse [5], [6], and child abuse homicides [7]. Clearly, understanding the connection between early neglect and long-term outcomes is an important public-health challenge.

Both human [8] and non-human [9] studies, separately and in combination, have contributed to the field's growing understanding of the neurological substrates and consequences of early neglect. Research among non-human species provides evidence of the pernicious effects of maternal deprivation on infant development. Behaviorally, maternal deprivation has been associated with marked deficits in the offspring's play behavior [10], high levels of social aggression [11], deficient cognitive functioning and learning [12], impaired social behaviours, increased emotional reactivity to novelty [13], and harmful and abusive parenting behaviors [14].

Whereas such deficits cannot be studied experimentally (i.e., manifested through experimental manipulations) among human young, adverse early experience, such as seen in institutional care, and parental neglect suggest similar effects [15], [16]. Children who have experienced early institutional care show the most pervasive negative outcomes [15]. Such children are often delayed in physical growth, show deficits in motor development [15] and extensive delays in cognitive functioning and language development [15]. In addition to developmental delays, institutionalized children often show highly anomalous behaviors, including stereotypies such as rocking, self-stimulating, and quasi-autistic behaviors. Their social behaviors are odd and often classified into one of two extremes— withdrawn and depressed in appearance, or indiscriminate in their attachment behaviors. Even high quality institutional care has deleterious effects on young children's development [16]. In general, children are not given the opportunity to develop selective attachment relationships to caregivers in institutions. A number of factors operate to make caring for children in institutions perfunctory. Institutional care seems to have specific adverse effects on children that other depriving conditions do not.

Yet, both human and non-human studies [17] suggest that there is rapid catch-up in physical and cognitive development following placement in enriched environments after even severe deprivation. Thus, adoptive placement in itself appears to represent a significant intervention with regard to physical and cognitive development catch-up [18], although problems persist among some children years after placement into adoptive homes [18].

To differentiate these positive and negative outcomes, researchers have been steadily engaged, especially since the 1990s in so-called international adoption studies with the aim of understanding why there is such a differentiation of outcomes, what pre-and post-adoption conditions differentiate these outcomes, and what individual differences, both in adoptees and in adoptive parents, matter for this differentiation. Specifically, numerous studies have followed developmental trajectories of children adopted both from institutions and foster families in lower-income and families in higher-income countries. For example, between 1999 and 2012, 242,602 (or ~20,000 annually) international children were adopted by families in the USA [19]. In general, families that pursue international adoption tend to be high-functioning, exhibiting a strong desire to care for children and higher-than-average socioeconomic background [20]. Thus, the socioeconomic variance between adoptive families is constrained and advantageous, compared to the socioeconomic conditions from which these adopted children originate.

Both the influx of international adoptions and the demand from educated adoptive parents to know more about the past, present, and future of their children has intensified the research field on international adoptions. Although multiple models of state care for children exist around the world, one of the dominant models of care is

institutionalization. Thus, a particularly interesting line of inquiry, in the US, Canada, and Western Europe, especially in the context of the studies mentioned above, has been research [21] into the developmental trajectories of so-called previously institutionalized (PI) children who were adopted internationally and now live in countries other than their birth countries, both when compared to themselves at their previous developmental stages and when compared to their peers adopted from foster families and living with their biological families in the country of origin and in their new adopted country [22].

Homo sapiens have evolved as an altricial species, meaning that early developmental stages of this species assume the presence of a caregiver, which is typically a biological parent (most often—a biological mother). In developmental sciences, there are convincing theoretical accounts [23] and empirical evidence [24] of the definitive impact of the presence/absence of such a caregiver and the quality of the child's dyadic relationships on the developmental trajectory of the child. Although, historically, foster care (i.e., placement of a child in either a biologically or communally related family) was established first as an alternative to orphanhood, institutional care had been the dominant *modus operandi* since the beginning of industrialization. Arguably, it is still the most prevalent form of care for orphan children, although relatively recently (since second half of the 20th century) numerous states have reverted to a foster care model, but a modified one, where the state offers financial and other incentives to foster care providers. Yet, it is important to note that it is not only the presence, but the quality of family care that is important. For example it has been shown that reunification of PI children with their biological families who were not committed to caring for their children did not correlate with cognitive gains; on the contrary, placement of PI children in adoptive families committed to caring for their adopted children correlated with cognitive gains [25].

It has been observed that, by definition (since in institutions children always outnumber adults which is often a reverse in modern families, where child care is distributed through multiple generations of adults), institutional care is characterized by suboptimal [26], compared to family care, features. For example, (a) care providers are personnel rather than parents, (b) low personnel-to-child ratios, (c) shift-based care arrangement; and (d) focus on the physical rather than the mental well-being of a child. Correspondingly, even under the best circumstances, with the systematic enhancement of practices [27], [28], institutional care is characterized as mostly adequate with regard to safety (including protection from different forms of abuse), medical care, sanitation, nutrition, and physical environment (equipment and toys) and mostly deficient with regard to social-emotional and other stimulating dyadic (i.e., individualized) interactions between the child and caregivers [29]. As family care is something that has been a component of the *Homo sapiens* evolution, its absence (no matter how well it is intended to be substituted by institutional care) is a major risk factor for various types of derailment from a typical developmental trajectory [30]. As many countries still primarily practice institutional care for orphans, many have mixed systems of care (e.g., Russia and China, where new legislative trends orient the system towards foster-family while maintaining institutional placement), and those countries that are primarily oriented toward family models adopt children from countries with dominating institutional care, it is important to qualify and quantify the impact of early institutionalization as a risk factor for subsequent development. Such qualification and quantification are important not only for developmental sciences, but also for families who consider fostering or adopting children with early institutional experiences and for pediatric practitioners (e.g., medical doctors, social workers, teachers) who work with these children throughout their lives.

Emerging elements of the collective portrait of the PI children, relative to their country of birth and adopted country peers, exhibit: (1) smaller body size, i.e., stature, weight, and head circumference [31]; (2) more delays in gross and fine motor development and muscle maturation [32]; (3) more cognitive vulnerability [33]; (4) more challenges in their speech and language development [33]; and (5) more susceptibility to health and mental-health problems [34]. These differences are especially pronounced prior to or at the time of adoption, but

diminish once placed with a new family [35], although many of them are never ameliorated completely [19].

Yet, in the majority of cases, summative prognosis for PI children are cautiously optimistic [29]. Specifically, the following observations have been made: (1) due to plasticity of the human brain, improving rearing conditions (as soon as possible) mends the outcome; (2) institutionalization does have a negative impact and it interacts, although it is not predisposed by, preexisting (i.e., genetic/genomic and prenatal/perinatal experiential) characteristics of the child; (3) although the general developmental trajectory impacted by early institutionalization can be mended, some developmental facets (e.g., linguistic, emotional, and volitional) are less acquiescent to normalization (these factors are assumed to be under stronger influences from other sources of individual differences, i.e., genetic/genomic). To illustrate, with regard to emotional development, as a group, PI children have been observed to have difficulties regulating emotions, interpreting facial expression and other social cues, forming secure attachment relationships with caregivers and suppressing “indiscriminant friendliness” and establishing successful intimate relationships [18], [25].

In understanding the impact of early institutionalization on child development, numerous moderating factors have been identified. One such factor in differentiating the impact of early institutionalization is the age of adoption [36]. There is a strong body of evidence suggesting that this factor is a strong protective factor, with children adopted early, on average, displaying much more “typical” developmental trajectories, and with fewer challenges across all facets of development. Another important factor is the severity of early adversity. Thus, there is evidence that this factor is associated with emergence and exacerbation of mental-health problems when PI children go through thresholds of major developmental transitions, such as those to adolescence [37] and adulthood [38]. A relevant concept in this context is that of allostatic load, i.e., the accumulation of physiological dysregulation that impedes, both qualitatively and quantitatively, typical developmental milestones [39].

Both the malleability of some and the resistance of other facets of development to normalization suggest the engagement of a biological substrate that substantiates both change and persistence of behavior. There is mounting evidence that multiple organs, tissue, and cell types respond to early adversity [18]. Moreover, there is empirically-based theoretical conviction in the literature that both the impact and the outcome of adversity are dependent on during whatever sensitive period (or periods) this impact occurs [40].

More specifically, early adverse experiences have been observed to modulate the offspring’s gene expression. This literature reveals associations of early care with the expression patterns of genes responsible for the production of such proteins as Brain Derived Neurotrophic Factor, BDNF [41], Gamma-AminoButyric Acid, GABA, oxytocin [42], estrogen [43], glucocorticoids [44], and other crucial players in the development, maturation, and functioning of the brain.

In addition, the last 10 years of research have generated an impressive amount of data connecting environmental adversity and human health through epigenetic mediation. The hypothesized mechanism assumes that cellular signaling pathways activated in response to these negative environmental conditions trigger long-term patterns of genome expression, and that these patterns, in turn, influence behavior and health (i.e., the phenotype of interest). In fact, the *epigenome* (i.e., the combined mechanism of deoxyribonucleic acid (DNA) methylation and chromatin modification that programs the differential expression of genes in different tissues) appears to be the mechanism that mediates the genome’s response to environmental signals (whether external or internal to the organism), modulating the interaction between environmental factors, genetic factors, and health outcomes. There is a considerable amount of literature connecting alterations of the epigenome to general health (e.g., cancer), but the role of epigenetic factors in mental health has only begun to be considered. The epigenome consists of chromatin and its modifications, and the methylation of cytosine rings found at the dinucleotide

sequence CG as well as in ribonucleic acid (RNA), specifically, in microRNAs and other noncoding RNAs [45].

It has been hypothesized that early adversity directly and indirectly affects the long-term expression pattern of critical genes involved in such early processes as immune regulation and function, stress reactivity, and the formation of social bonding, affiliation, and attachment through epigenetic reprogramming. Although some preliminary evidence has been secured for this hypothesis [46], it makes several assumptions that need to be tested. (1) Early social environment alters epigenetic states in humans systemically in several tissues, and these are measurable in peripheral lymphocytes, specifically through DNA methylation signatures; as epigenetic states are tissue specific, we anticipate that some of the changes in DNA methylation will be unique to different tissues whereas others will be common to several tissues. (2) Different epigenetic states are related to altered gene expression in important pathways that, in turn, affect behavior and physiology later in life. (3) These epigenetic states may be altered by social interventions.

As the evidence has accumulated to indicate that early adverse experiences are serious risk factors for subsequent development, the field needs to understand the biological machineries that are triggered by these experiences and that may be protective of normative developmental milestones. Understanding these complex interplays is in the realm of new directions of psychological research and practice—those that have recently emerged at the junction of psychological and genomic sciences and that will, inevitably, rapidly develop in the very near future.

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